REMARKS

Claims 46-65 were pending in the present application. Claim 60 has been canceled without prejudice. Applicants reserve the right to pursue the subject matter of the canceled claim in one or more related applications.

Claim 46 has been amended to clarify that which Applicants regard as the invention. Specifically, claim 46 has been amended to recite that the saponin adjuvant is a *Quillaja saponaria* saponin adjuvant. Support for this amendment can be found in the specification, for example, at page 5, lines 30-31. Claim 46 has been further amended to delete recitation of "human serum albumin." These amendments are made without prejudice. Applicants reserve the right to prosecute the deleted subject matter in related applications.

Applicants have amended claim 54 to delete "peptide" and "protein." This deleted subject matter has been included in new claim 67. New claim 68 has been added to correspond to claim 65 in view of the amendments to claim 54.

Claim 55 has been amended to delete "Polysorbate," since this subject matter is now claimed in claim 56. Claim 56 has been amended to be dependent upon claim 46. Claim 63 has been amended to be dependent upon 52 in addition to being dependent upon claim 46. Claim 65 has been amended to delete dependency upon claim 63, in order to avoid having a multiply dependent claim depend upon a multiply dependent claim. New claim 66 has been added to correspond to claim 65 in view of the amendment to claim 65.

No new matter has been added by these amendments. Upon entry of these amendments, claims 46-59 and 61-68 will be pending in the present application.

Applicants respectfully request that the amendments and remarks made herein be entered and fully considered.

INTERVIEW SUMMARY RECORD

Applicants and Applicants' representatives wish to thank Primary Examiner Patrick J. Nolan and Examiner Yunsoo Kim for the courtesy of the telephonic interview of August 9, 2005 with Applicant's representatives, Adriane M. Antler, Gojeb L. Frehywot and Henry P. Wu, in connection with the above-referenced application.

During the Interview, Dr. Antler presented reasons as to why the claimed invention was nonobvious over the references cited by the Examiner, i.e., U.S. Patent No. 5,057,540 and U.S. Patent No. 4,772,466 (as described in detail below). Agreement was reached on the possible withdrawal of the § 103 rejection.

Primary Examiner Nolan brought U.S. Patent Nos. 4,788,056 (col. 2, lines 53-65) and 5,688,772 (cols. 11-12, overlapping paragraph) to Applicants' attention. Attorneys

for Applicants agreed to consider the references in their response. The references are discussed below.

The Rejection Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 46-57 and 63-65 stand rejected under 35 U.S.C. § 103(a) as being obvious over Kensil et al. (U.S. Patent No. 5,057,540; "Kensil") and Allison et al. (U.S. Patent No. 4,772,466; "Allison"). Applicants respectfully disagree with the Examiner's rejection and submit that the rejection should be withdrawn for the reasons discussed below.

The Examiner contends that Allison teaches that non-ionic surfactants, including polysorbate, polysorbate 20, polysorbate 80 (col. 6, lines 46-48) and other sorbitan-based non-ionic surfactants are very useful in vaccine formulations since they increase the efficacy of the vaccine compositions and stabilize the emulsion when a suspension is formed (cols. 4-6).

The Examiner further contends that Allison teaches combining a non-ionic surfactant such as Pluronic® with a saponin adjuvant to increase protection (Example 4). The Examiner also contends that Allison teaches that a non-ionic surfactant is non-toxic and may be safely used as a vehicle for enhancing immunogenicity and Allison states that TWEEN® is the most preferred surfactant.

The legal standard for nonobviousness was presented in Applicants' Amendment Under 37 C.F.R. 1.111 filed on April 11, 2005. The teachings of Kensil and Allison were summarized in Applicants' Amendment Under 37 C.F.R. 1.111 filed on April 11, 2005.

With respect to the bases for the Examiner's rejection, relating to combining a non-ionic surfactant with a saponin adjuvant, Applicants respectfully disagree and submit that the presently claimed invention is not obvious because neither Kensil nor Allison provide a suggestion or motivation to use a non-ionic surfactant such as Polysorbate or Triton X-100 with a saponin adjuvant.

The invention in Allison relates to improved means for potentiating the immunogenicity of antigens. See Allison at col. 2, lines 4-5 and col. 2, lines 66 to col. 3, line 6. A new adjuvant is described therein, i.e., an emulsified glycopeptide, block polymer and non-ionic surfactant. In Allison, the block polymer is critical to the immune response. See Allison, col. 2, lines 30-31. The use of the non-ionic surfactant is Allison is specific to the composition described. In particular, the non-ionic surfactant stabilizes the block polymer in a multiphase system. See Allison, col. 2. lines 31-34.

This new adjuvant described by Allison was contrasted with the prior art saponin adjuvant. In particular, Example 4 of Allison compares a standard adjuvant (aluminum hydroxide and Quil-A®) with the Pluronic®-based adjuvant of the invention. See Allison at col. 13, lines 60-63. Contrary to the Examiner's contention, the Pluronic®-based adjuvant is not combined with the saponin Quil-A®. Allison's characterization of the results also make clear that the example describes the comparison of the results achieved using the Pluronic®-based adjuvant to the results achieved using the aluminum hydroxide/Quil-A® adjuvant, not the combination of a Pluronic®-based adjuvant with a saponin adjuvant. See Allison at col. 15, lines 26-29.

Thus, contrary to the Examiner's suggestion, Allison does not teach or suggest the desirability of using an emulsifying or suspending agent, such as a polysorbate, with a saponin adjuvant. Kensil does not rectify this deficiency, since it also does not suggest combining a non-ionic surfactant (or a β-cyclodextrin or deacylsaponin) with a saponin.

Kensil discloses the use of bovine serum albumin (BSA) as an antigen in combination with certain *Quillaja saponaria* saponins (see Fig. 15 and Example 15). While there is no suggestion of using human serum albumin (HSA) in Kensil, nevertheless, Applicants' claims no longer recite "human serum albumin." Thus, this disclosure by Kensil is irrelevant to the patentability of the claimed invention.

Allison, whether alone or in combination with Kensil, does not render obvious the presently claimed invention. Accordingly, the references cited by the Examiner do not provide a *prima facie* case of obviousness.

In view of the foregoing, Applicants respectfully assert that the rejection of the pending claims under 35 U.S.C. § 103(a) is in error and respectfully request that the rejection be withdrawn.

Discussion of Additional References

U.S. Patent No. 4,788,056 to Lütticken et al. ("Lütticken") relates to combined vaccines for viral and bacterial infections. The vaccines described by Lütticken contain immunogenic *E. coli* material and viral material. The vaccine may also contain additional components such as adjuvants including saponin. Lütticken discloses three instances of the use of saponin (col. 2, lines 53-66):

1. as an example of an adjuvant that can be used, in a list also containing examples of other adjuvants such as aluminum salts, $Ca_3(PO_4)_2$, DDA, etc.;

2. in combination with a water-in-oil emulsion (saponin is listed as an *alternative* to Polysorbate 80); and

3. in combination with a gelatin or hydroxpropylmethylcellulose phthalate in the form of capsules.

Lütticken does not teach, either expressly or inherently, the combination of Polysorbate 80 and saponin. Since Lütticken does not teach each and element of the present claims, Lütticken does not anticipate the present claims.[1] Moreover, there is no suggestion of the combination of Polysorbate 80 and saponin, and thus Lütticken cannot render obvious the claimed invention.

Lütticken mentions the use of serum proteins/albumins at col. 2, lines 5-8 and 24-29; however, since "human serum albumin" has been deleted from the claims, this disclosure by Lütticken does not affect patentability of the claims.

U.S. Patent No. 5,688,772 to Estrada et al. ("Estrada") discloses a comparison of *Quillaja saponaria* saponin and Quinoa saponin (Example I; cols. 9-11). However, there is no suggestion in Estrada of combining *Quillaja saponaria* saponins with a non-ionic surfactant (or a β-cyclodextrin or deacylsaponin). Estrada also discloses that some antigens will benefit by being coupled to a carrier molecule such as a serum albumin (col. 8, lines 18-23). Estrada also discloses administration of an antigen-saponin preparation of human serum albumin radiolabeled with technetium and a saponin preparation from *Chenopodium quinoa* (see Example II, cols. 11-12). In an effort to expedite prosecution of the present application, Applicants have amended claim 46 to delete recitation of a human serum albumin, and canceled claim 60. Estrada thus does not anticipate or make obvious the claimed invention.

[1] "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). See MPEP § 2131.

CONCLUSION

Applicants respectfully request that the present amendments and remarks be made of record in the instant application. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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